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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,501	04/22/2002	Hiroyuki Saito	053466-0325	9449

22428 7590 12/27/2006
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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	PAPER NUMBER
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/27/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/089,501	SAITO ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-54* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-54* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Receipt and entry of the amendment dated 10/5/2006 is acknowledged. After entry of the amendment, claims 45-54 are pending and under examination.

Claim Objections

Claim 54 is objected to because of the following informalities: "parings" should be "pairings." Appropriate correction is required.

Specification

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: claim 1 has been amended to recite growth of blood vessels "caused by expression of tissue factor" and an antibody having "neutralizing activity" to human tissue factor. Applicant does not indicate where in the specification support for the amendments may be found. Neither of the phrases "caused by expression of tissue factor" nor "neutralizing activity" are found within the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-54 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not

described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 51 has been amended to recite antibodies chosen from the group of "the antibody heavy and light chain pairings of" various SEQ ID NOs. Applicants do not indicate where in the disclosure support might be found for the amendment. A reading of the specification reveals that the SEQ ID NOs cited only comprise the V regions of various antibodies (see Tables 1-3). Therefore, the recited antibodies comprise only the heavy and light chain V regions. There is no disclosure of such antibodies in the specification, much less the versions (i.e. b-b, i-b, or i-b2) recited in the claim, which are chimeric IgG molecules (see Examples 6 and 7). Thus, the amended claims include impermissible New Matter. **This is a new rejection necessitated by amendment of the claims. This is a New Matter rejection.**

Claim 45 (from which all other claims depend) recites a method for "suppressing the growth of blood vessel tissues in a patient in need thereof." Thus, the claimed subject matter includes treatment of angiogenesis and neovascularization, in addition to stenosis and restenosis. The specification presents an Example wherein pre-treatment with the i-b2 monoclonal antibody suppressed growth of the blood vessel lumen (i.e. intima) in response to physical injury. While this is a single example of treatment of restenosis, it does not provide support for angiogenesis or neovascularization. A review of the specification reveals no disclosure, or contemplation, of treating disease other than restenosis. Thus, the claims include impermissible New Matter. **This rejection is maintained for reasons made of record in the previous Office Action and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 10/5/2006 have been fully considered but they are not persuasive. Applicants essentially assert that Example 6 provides support for the claimed subject matter on page 41, lines 10 and 11. The passage reads:

> *"This indicated that humanized anti-human TF antibody "version i-b2" prevents the narrowing of the area of the lumen during the remote period by suppressing growth of the blood vessel tissue itself, suggesting that it can effectively prevent restenosis."*

As indicated in the previous Office Action, this passage only provides support for the treatment of restonosis, and no other disease. Furthermore, it only provides support for preventing narrowing of the lumen, not a general inhibition of blood vessel growth, such general inhibition being only a speculation. There is nothing in this passage, or the remainder of the specification, to lead one of skill in the art to use the i-b2 antibody (or any other anti-TF antibody) to suppress blood vessel growth associated with any disease other than restonosis.

Claims 45-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using human TF antibodies to suppress restenosis, does not reasonably provide enablement for using human TF antibodies to suppress any other types of blood vessel growth, e.g. angiogenesis or neovascularization. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims broadly recite a method of inhibiting blood vessel growth by administration of human TF antibodies. Types of blood vessel growth include stenosis, restenosis, angiogenesis, and neovascularization. The instant

specification discloses the use of one human TF monoclonal antibody (i-b2) to suppress restenosis, and does not mention the use of human TF antibodies to suppress blood vessel growth related to angiogenesis or neovascularization. **This rejection is maintained for reasons made of record in the previous Office Action and for reasons set forth below.**

Response to Arguments

Applicant's arguments filed 10/5/2006 have been fully considered but they are not persuasive. Applicants essentially assert that: 1) a high level of skill in the art, in the form of animal models and assays, existed at the time of filing; 2) it was known that growth of blood vessels causes restonosis, angiogenesis, and neovascularization; 3) tissue factor controls the balance of tumor cell activities; 4) tissue factor has an integral role in tumor biology; and, 5) given the models and assays present in the art and the knowledge of the role of tissue factor in tumor biology, one of skill could have practiced the claimed invention without undue experimentation. Applicants cite Zhang et al in support for 2)-4) above.

Regarding 1) and 5), that relevant models and assays exist is not in dispute, but it does not equate to teaching how to make and use an anti-TF antibody that suppresses angiogenesis or neovascularization. It only means that if one of skill in the art had such an antibody, it could be tested. In the alternative, it means that the tools exist for one of skill in the art to conduct lengthy and repetitive experiments to prepare and isolate such an antibody themselves (if such an antibody is indeed possible) because applicants have not done so. Merely binding to TF does not equate with the claimed functionality, as demonstrated by applicants: the b-b and i-b antibodies bind TF, but did not inhibit restonosis. Therefore, in order to make and use an antibody according to the instant claims that suppresses angiogenesis, it is not merely a matter of

preparing anti-TF antibodies. Regarding 2), this is not in dispute, and is indeed a point of this scope of enablement rejection. Regarding 3) and 4), again, these facts are not in dispute, but it remains to be shown that an anti-TF antibody could inhibit the activity of TF responsible for angiogenesis. The role of TF in tumor biology is completely independent from its role in coagulation/restonosis. This is supported by Zhang et al (cited by applicants, Exhibit A), who teach that the role of TF in angiogenesis and tumor biology is due to an increase in growth regulatory molecules, a mechanism distinct from its activation of coagulation (see last sentence of the abstract and page 1326, ¶ bridging first and second columns). Thus, it is easy to envision that whereas certain anti-TF antibodies may inhibit coagulation or restonosis, the same antibodies do not necessarily inhibit blood vessel growth in general. Therefore, it is unpredictable that anti-TF antibodies would suppress angiogenesis or neovascularization, and it would require undue experimentation to make and use such antibodies, if it is indeed possible to make them.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

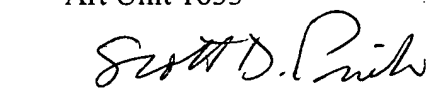
the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart
Examiner
Art Unit 1633



SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER